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# Is there an upper limit to the risks that humanitarian research may legitimately visit upon research participants?

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*Ethics and Humanitarian Research: Generating Evidence Ethically*

Nir Eyal declares having no relevant conflicts of interests.

# Today's talk

I. Introduction

II. Characterizing the notion of caps on legitimate risk to humanitarian research study participants

III. My arguments *against* such caps

IV. Addressing others' arguments *for* such caps

# I. Introduction

# Leading bioethicists express support for “upper limits”/caps on acceptable risk in research

- Frank Miller and Steve Joffe?
- Alex London
- Annette Rid and Dave Wendler
- David Resnik

# When no benefit for participants expected, many research ethics guidelines/regs espouse caps on risk:

- E.g. U.S. Department of Health and Human Services (DHHS) 2009; Emanuel et al. 2000; Council for International Organizations of Medical Sciences (CIOMS) 2002; South African Medical Research Council (SAMRC) 2002; Council of Europe (CoE) 2005; Indian Council of Medical Research (ICMR) 2006; Ad hoc group for the development of implementing guidelines for Directive 2001/20/EC (Ad hoc group) 2008; Schweizerische Akademie der Medizinischen Wissenschaften (SAMW) 2009; Schweizerische Eidgenossenschaft, Bundesamt für Gesundheit (BAG) 2011; World Medical Association (WMA) 2013 (Rid 2014).
  - + when participants' valid consent unobtainable, such caps are *low* (Rid 2014).
  - + when some benefits are expected, many would nonetheless condemn some studies of tremendous social value as, on balance, too risky for participants.
  - + for some research ethicists, the cap on net-risk from study participation should be  $\leq 0$ .

In short, many authors and guidelines would/should endorse:

- *Caps on acceptable risk:* There is a level or a kind of risk such that visiting it upon study participants for study purposes alone is never permitted, no matter how socially important the study is.
- Let me further characterize this position, before we turn to its critique.

II. Characterizing the notion of  
caps on legitimate risk to to  
humanitarian research study  
participants



Only studies in the grey area are justified at the bar of a favorable risk/benefit balance.

*Social value*

**a**

**d**

**c**

**b**

No risk

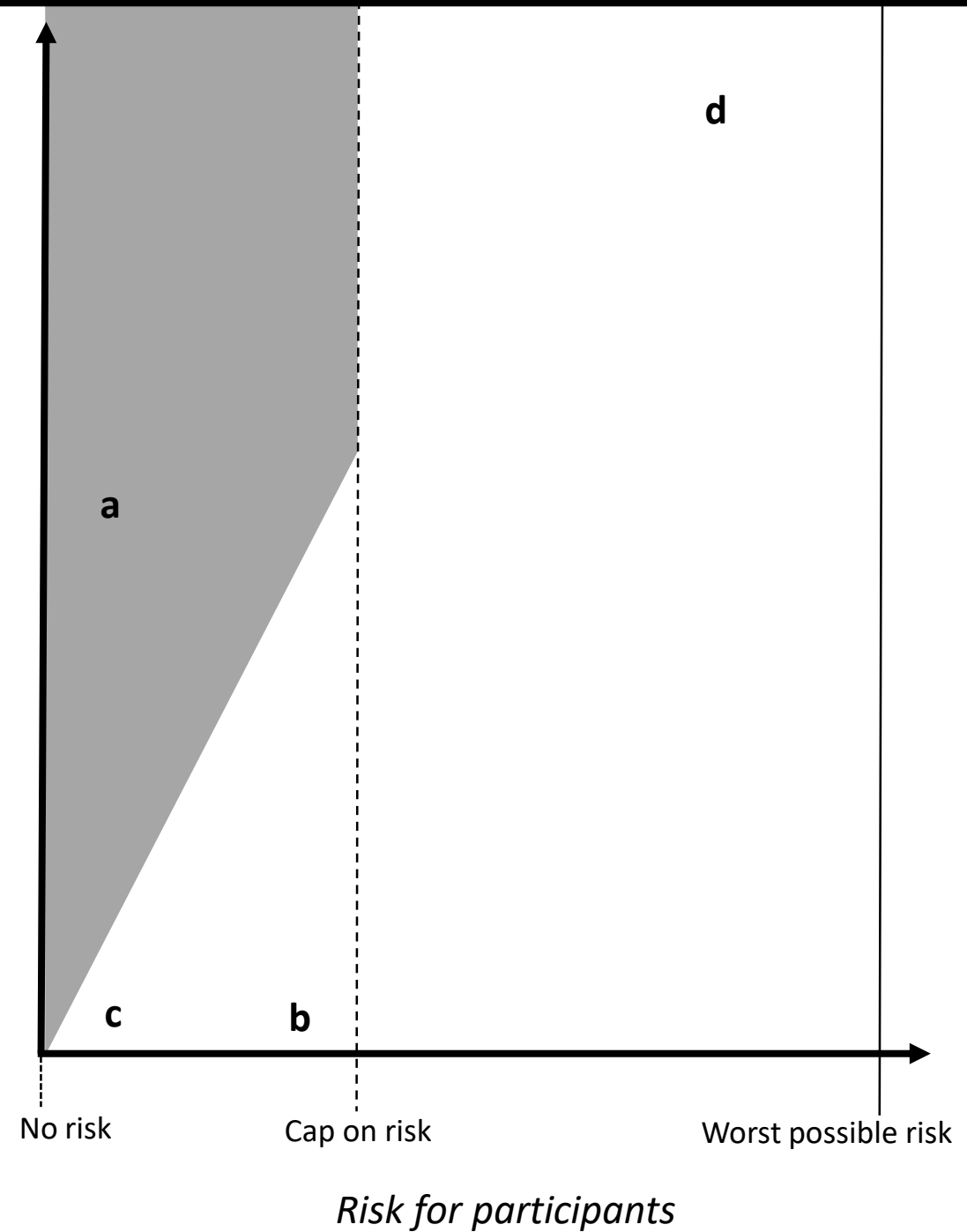
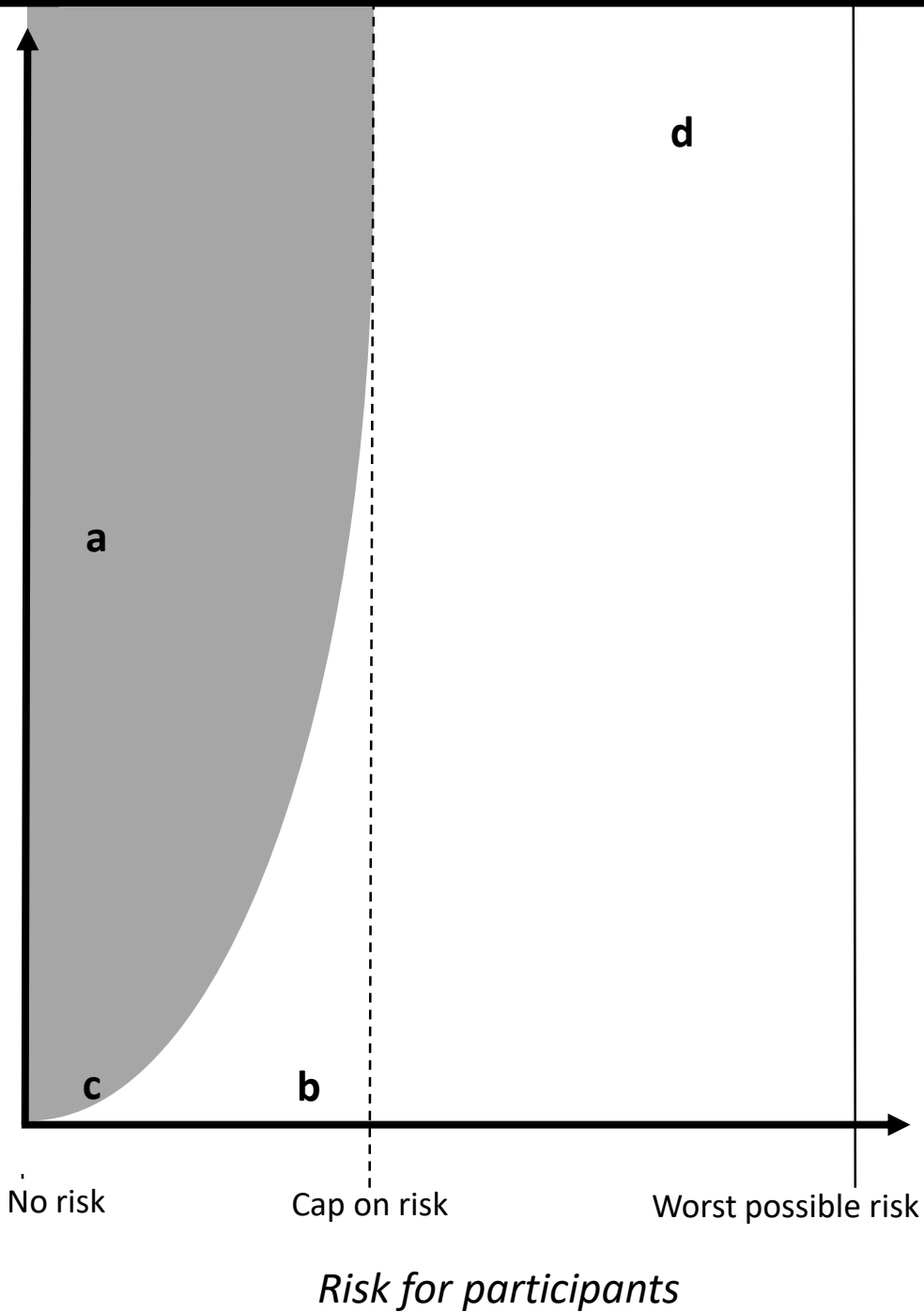
Worst possible risk

*Risk for participants*

*Views that  
reject a  
cap on  
study risk to  
participants*

*Views that  
accept a  
cap on  
study risk to  
participants*

*Social value*



### III. My arguments against caps on risk in humanitarian research

# Four arguments against caps on risk in humanitarian research

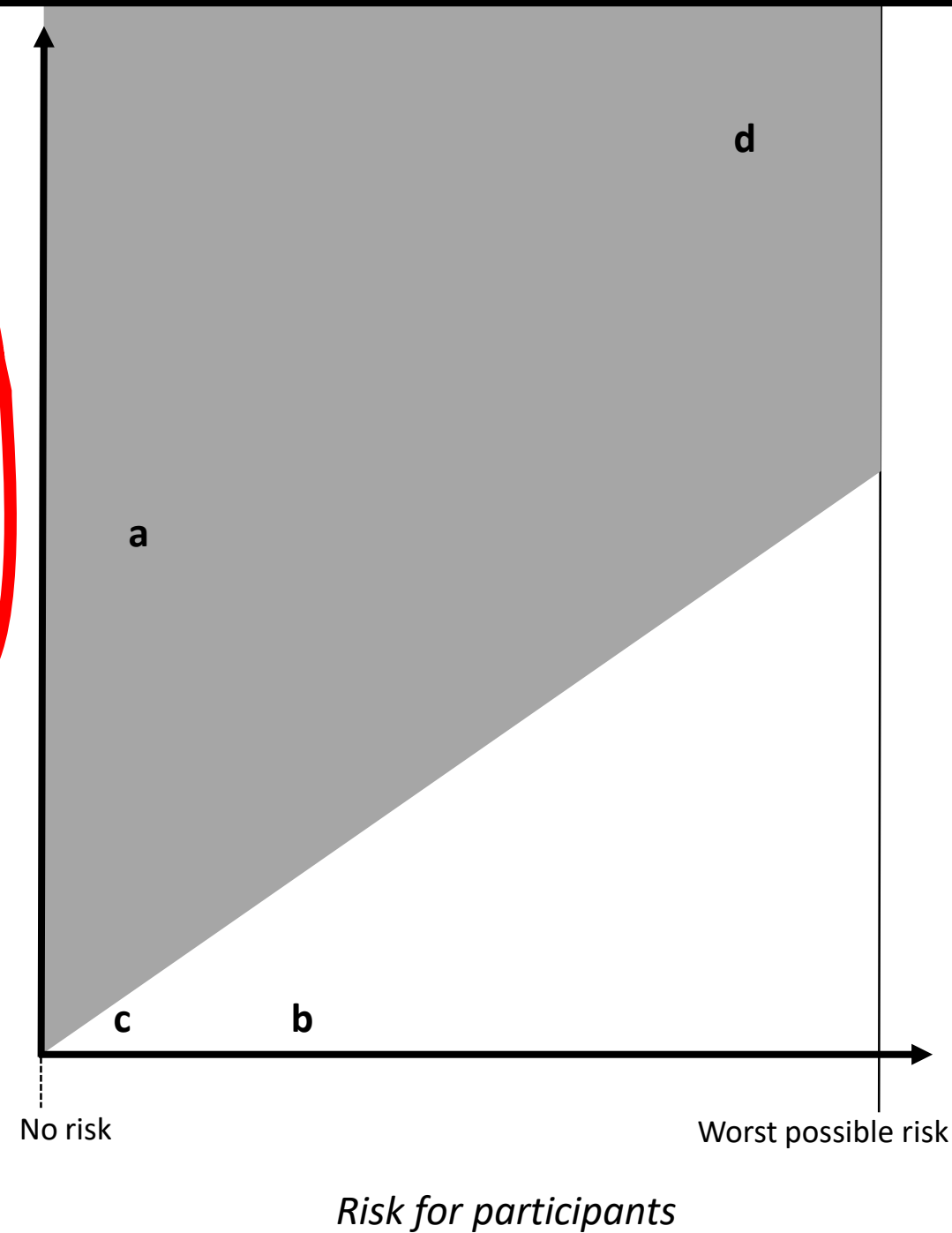
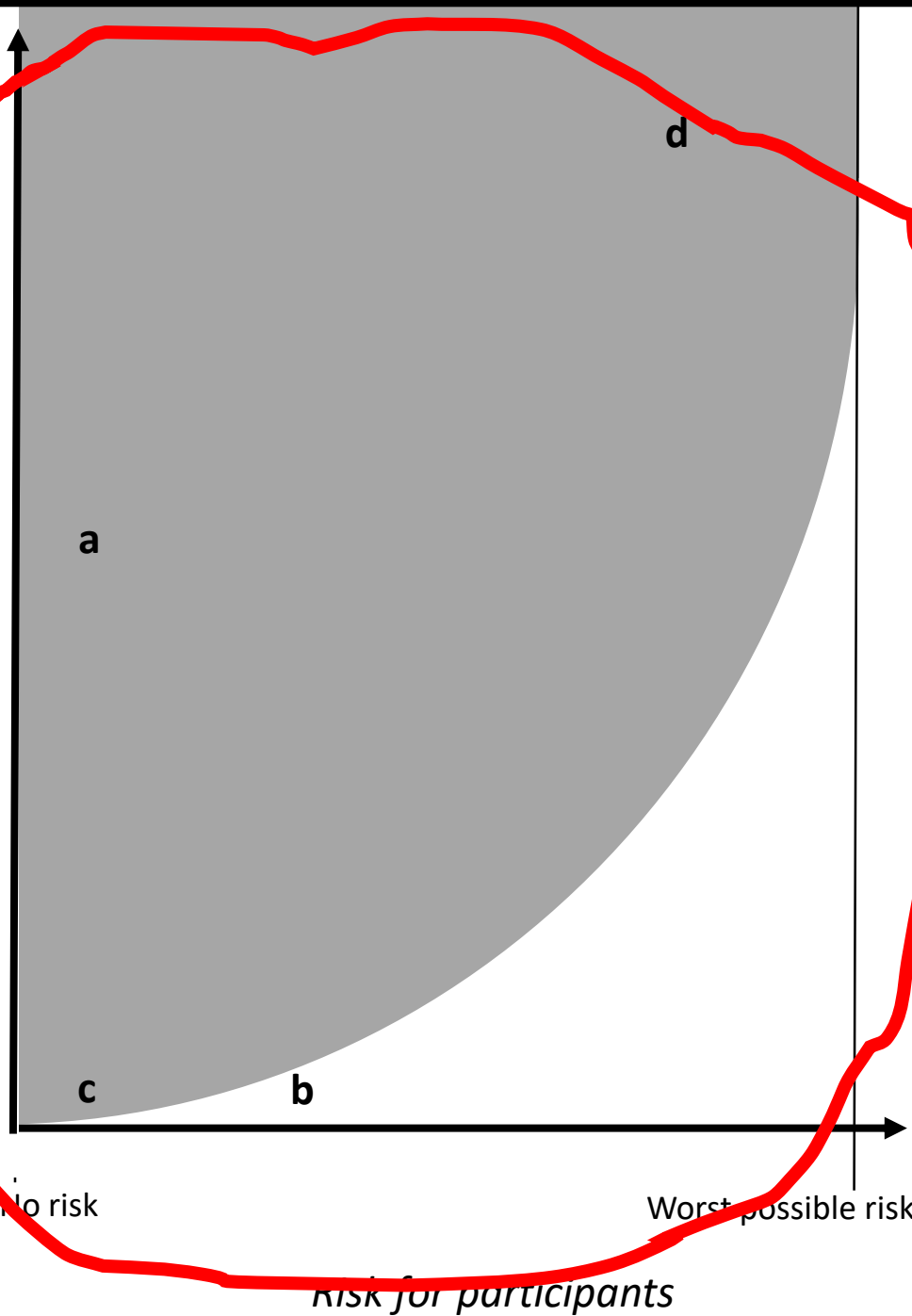
1. Anti-absolutism
2. Caps' initial intuitive appeal wanes in concrete cases
3. Medically high risk studies can remain (nearly) beneficial overall—even in health terms.
4. Consent

# 1. Anti-absolutism

- Caps on risky medical studies constitute an absolute prohibition.
- But nearly all contemporary ethicists reject absolute prohibitions.

Views that  
*reject a*  
cap on  
study risk to  
participants

*Social value*



## 2. Caps' initial intuitive appeal wanes in concrete cases

- an outbreak of a highly infectious, extremely lethal strain of MERS starts at a civil war zone. Either standard containment strategies or investigating the efficacy of a safety-tested vaccine candidate in the field are impossible in that dangerous zone, which people flee to many international destinations. This creates a dilemma, between:
  1. deferring vax efficacy testing till the outbreak reaches other areas (risks millions of lives);
  2. inviting a small number of volunteers now to receive the candidate vaccine and then be exposed to the relevant MERS strain vs. placebo control.
    - The latter study would be extremely risky for volunteers in either arm.
      - Because strain is very lethal & candidate vax, merely experimental & offered only in 1 arm.
    - But the study would accelerate effective response—with extreme societal value.

# A clarification about the case

- Animal challenge studies to test the efficacy of this vaccine candidate for this MERS strain would have been a third option. But assume:
  - such studies were already conducted and found this candidate efficacious in some species and inefficacious in others; and/or
  - current knowledge suggests that the vaccine candidate would work very differently in humans than in virtually all animal models.
- In addition, animal studies take time, which, in the circumstances, could also translate into many, many human lives.



### 3. Medically high risk studies can remain (nearly) beneficial overall—even in health terms.

- E.g. invitations to participate could be targeted at *healthy* people who are at high risk of getting infected, e.g. healthy contacts of contacts of an infected person.
  - For such people, if the investigational vaccine turns out to work, they could be protected from an otherwise-likely extremely lethal infection.

## 4. Consent

- When philosophers discuss the famous counterexamples to utilitarianism (footbridge examples, transplant examples, the Jim and the Indians case, the Georgia lynch example, and many others), these usually involve risk/harm to an individual who is *not* consenting to be put at risk/harm.
- When the individual consents to take on a risk, as study participants do in the case above, that should make a big ethical difference.
  - Indeed, there is a real question as to whether barring that person from taking on that risk isn't too paternalistic.
- Consent to taking on an extreme net risk need not be irrational/uninformed/invalid, when the social benefits are tremendous.

## IV. Addressing arguments for caps on risky humanitarian research

## IV. Responding to arguments for caps on risky humanitarian research

1. To "in real-life examples, the social value of studies is never certain"
2. To London's "principle of equality"
3. To London's concern about loss of trust
4. To the specter of historical abuses
5. To concerns about potential (perceived) abuse

Responding to argument 1, Viz. "in real life, the social value of studies is never certain"

- It is true that there is never certainty in clinical trials.
- But a back of the envelope calculation shows that at least in our MERS case, societal value can be far greater than what is usually conceived as the plausible deontological threshold.
  - Exp. social value: 50 million /
  - Exp. risk to volunteers:
    - $87,500 / 22 = \sim\mathbf{3,977}$ .
  - **$\sim\mathbf{3,977}$**  is  $\sim 100$  to  $200$  times prevalent thresholds for permitting the killing of one nonconsenting innocent to prevent others from dying.

# Responding to argument 2, Viz. London's "principle of equality"

For London, "as a necessary condition for ethical permissibility, research with human subjects must be designed and carried out so as not to undermine the standing of research participants as the moral and political equals of their compatriots, by either knowingly compromising their basic interests or showing unequal concern for their basic interests and the interests of the people the research is intended to serve" (London 2009).

- But as objection to extreme-risk trials, London's principle rules out even:
  - Many accepted trials with net-negative prospects for participants, e.g. toxicity trials.
  - By implication, some legitimate policies outside medical research:
    - rationing of health resources
    - redistributive taxation

# Responding to argument 3, Viz. London's concern about loss of trust

London points out that risky research jeopardizes “the willingness of community members to believe the information that they receive from basic social and governmental institutions, to rely on and comply with their instructions, and to provide various forms of cooperation and support for their efforts” (London 2009).

- But socially highly valuable experiments can also *promote* trust.
- Such experiments may also make so much headway against the infection as to warrant on balance some risk of decline in public trust.
- London may imagine that public trust is fully destroyed so easily that he would have to condemn widely-used disaster response measures.

# Responding to argument 4, Viz. the specter of historical abuses

- Logically, the fact that many highly abusive studies contained a certain element, e.g. very high risk to participants, does not show that every study containing that element is abusive.



# Responding to argument 5, Viz. concerns about potential (perceived) abuse

- Other protections can provide the necessary assurances that the permission to conduct highly risky studies is not abused.
  - No need to bar ourselves from conducting these studies when most needed.

# Conclusion

- To be able to fight threats to public health as effectively and expediently as we can in humanitarian research, let's reject Caps on Acceptable Risk.
  - Study participants should instead be protected by other requirements from humanitarian researchers.